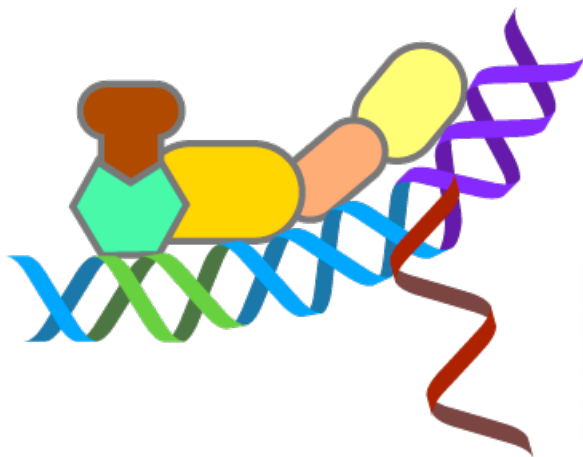


Understanding Cancer and Related Topics

Understanding Estrogen Receptors, Tamoxifen, and Raloxifene



Developed by:
Lewis J. Kleinsmith, Ph.D.
Donna Kerrigan, M.S.
Jeanne Kelly

Describes the hormone estrogen and its receptor. Explains the relationship of estrogen and its receptor to breast cancer and the risks and benefits of reducing cancer risk with drugs called antiestrogens and selective estrogen receptor molecules (SERMs).

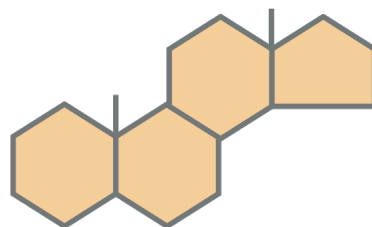
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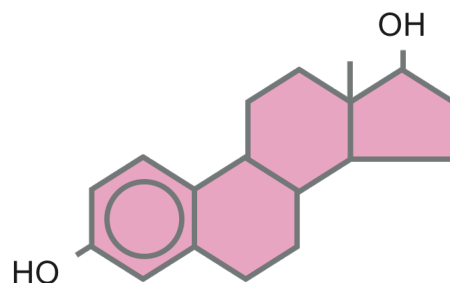
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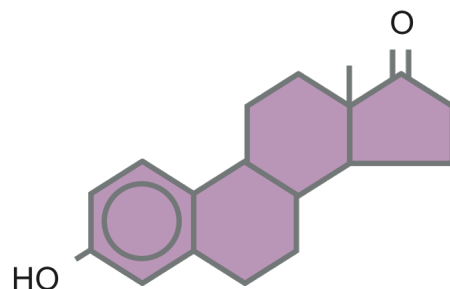
What Are Estrogens?



Steroid ring system



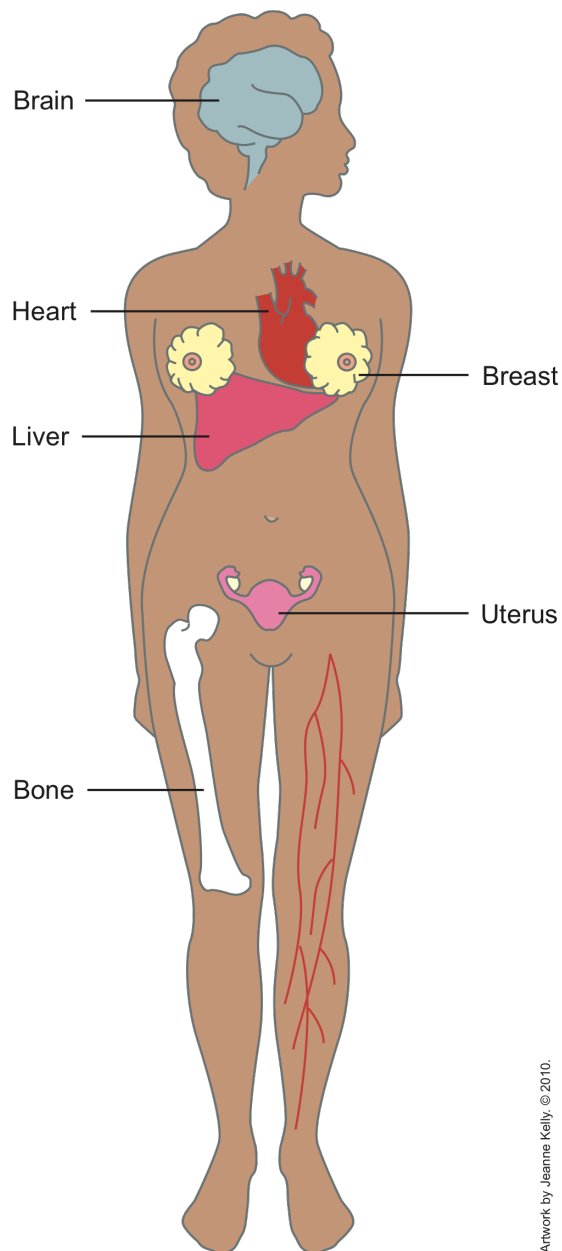
Estradiol



Estrone

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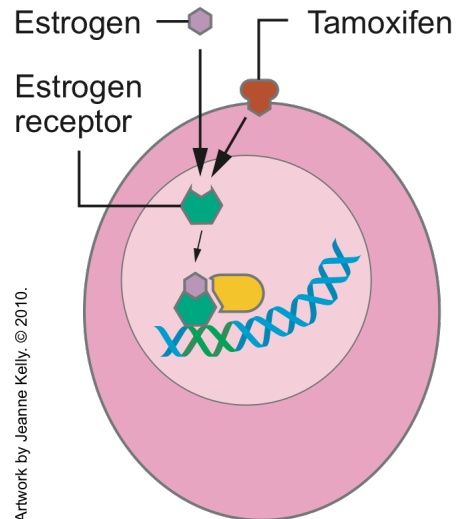
Estrogen Targets Tissues



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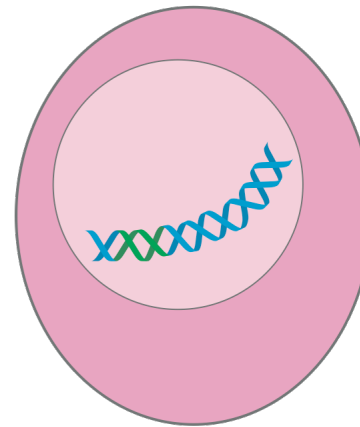
Estrogen Receptors

Estrogen target cell
(e.g., breast, uterine lining,
liver, etc.)



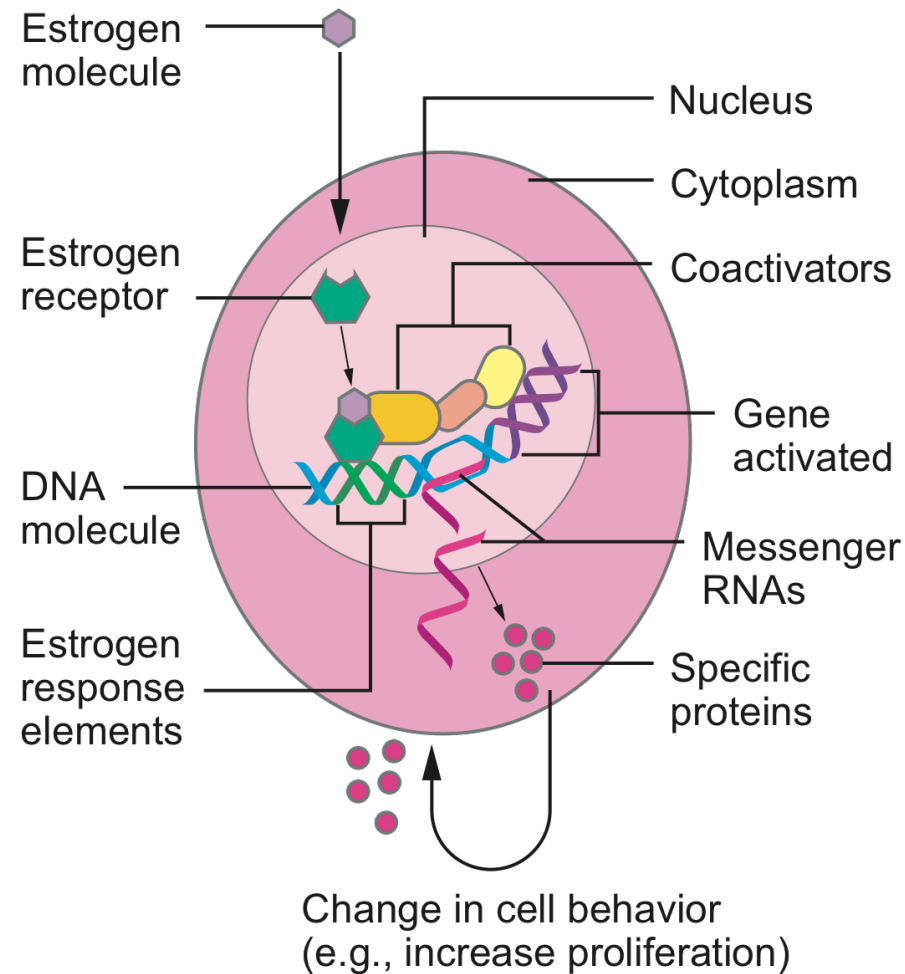
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Non-target cell
(contains no
estrogen receptor)



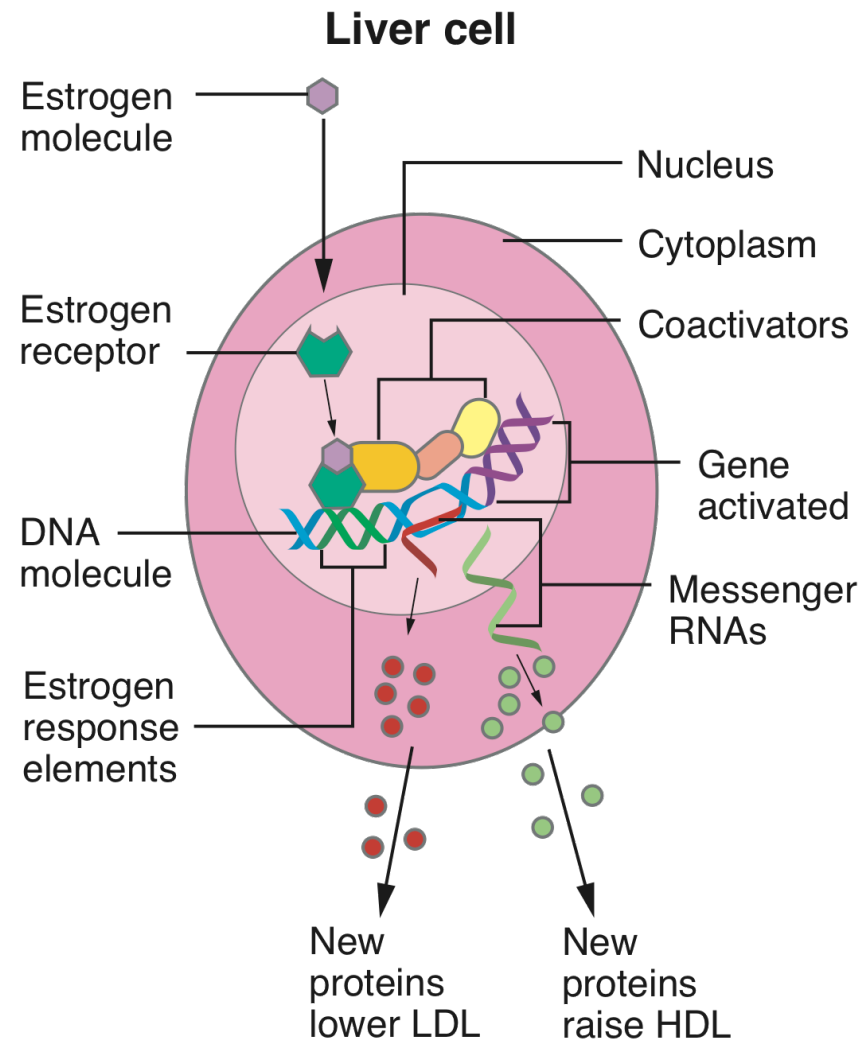
Estrogen Receptors

Trigger Gene Activation



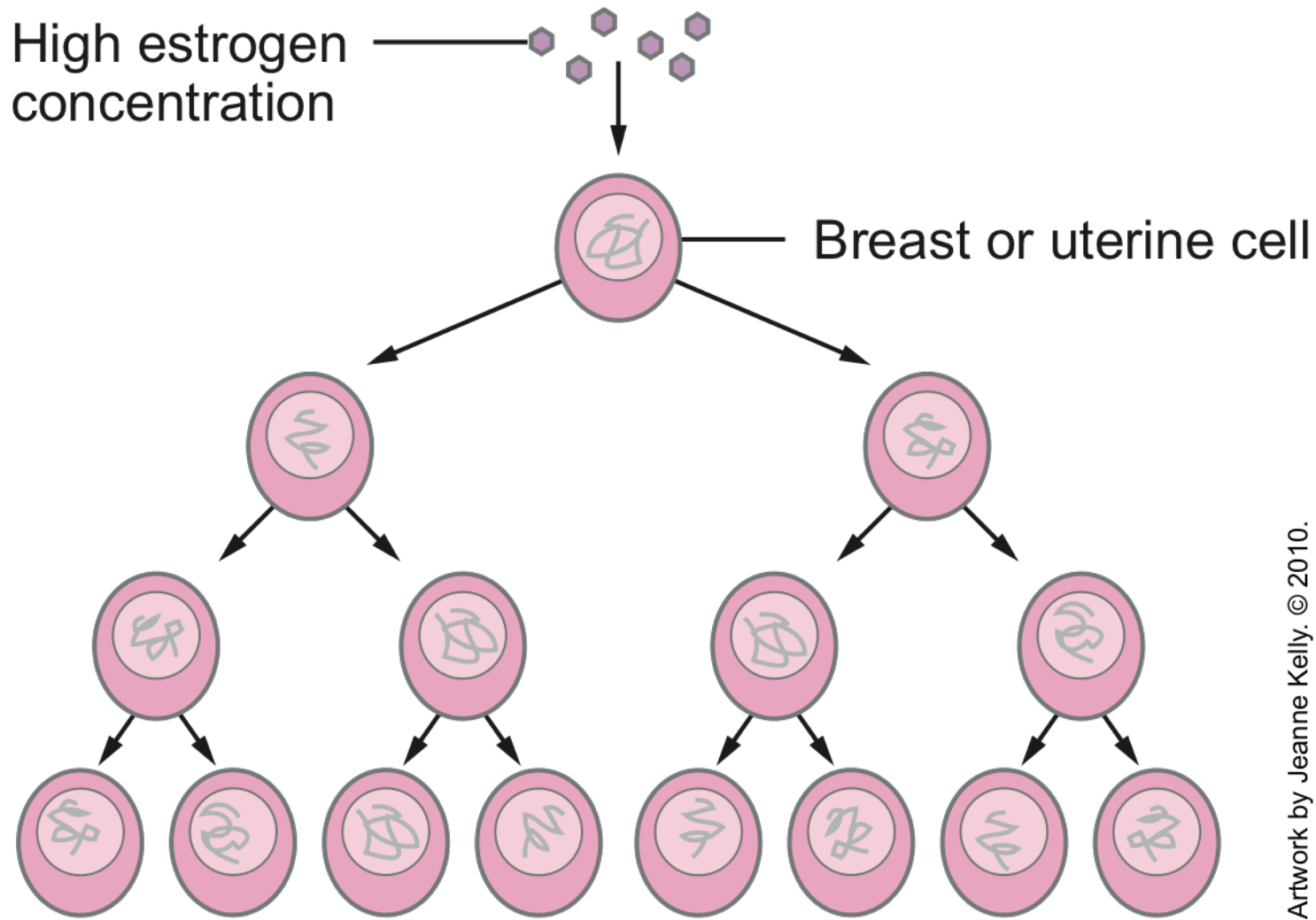
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Estrogen-Induced Changes in Cell Behavior



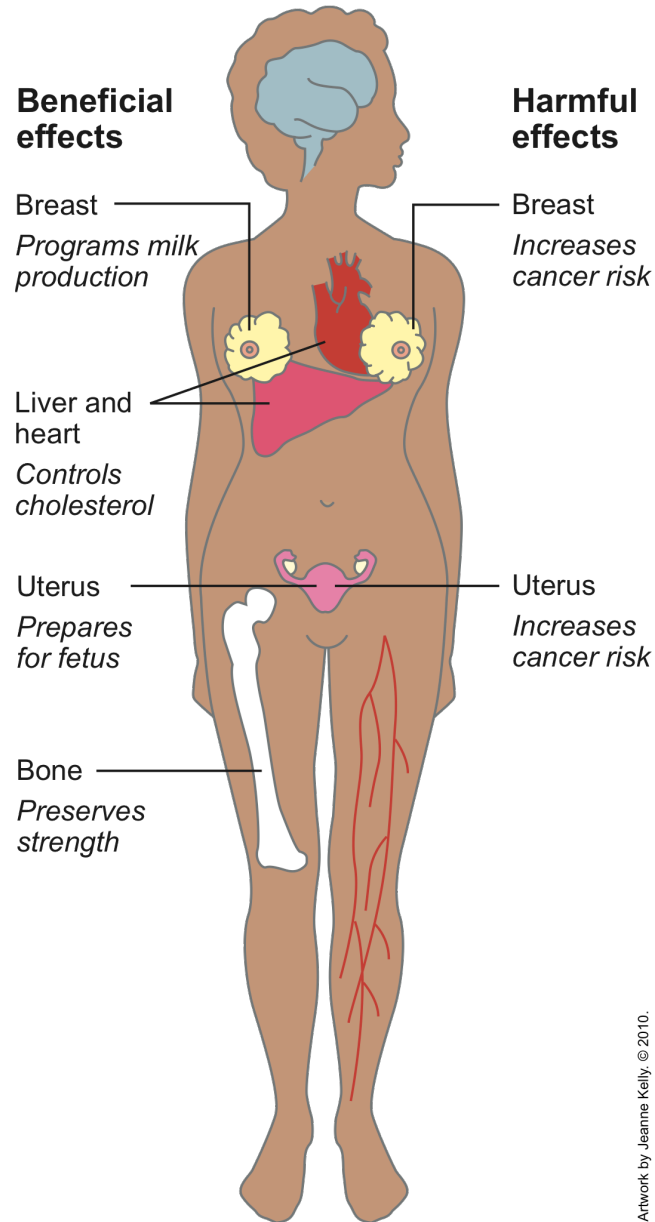
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Estrogen-Induced Stimulation of Cell Proliferation



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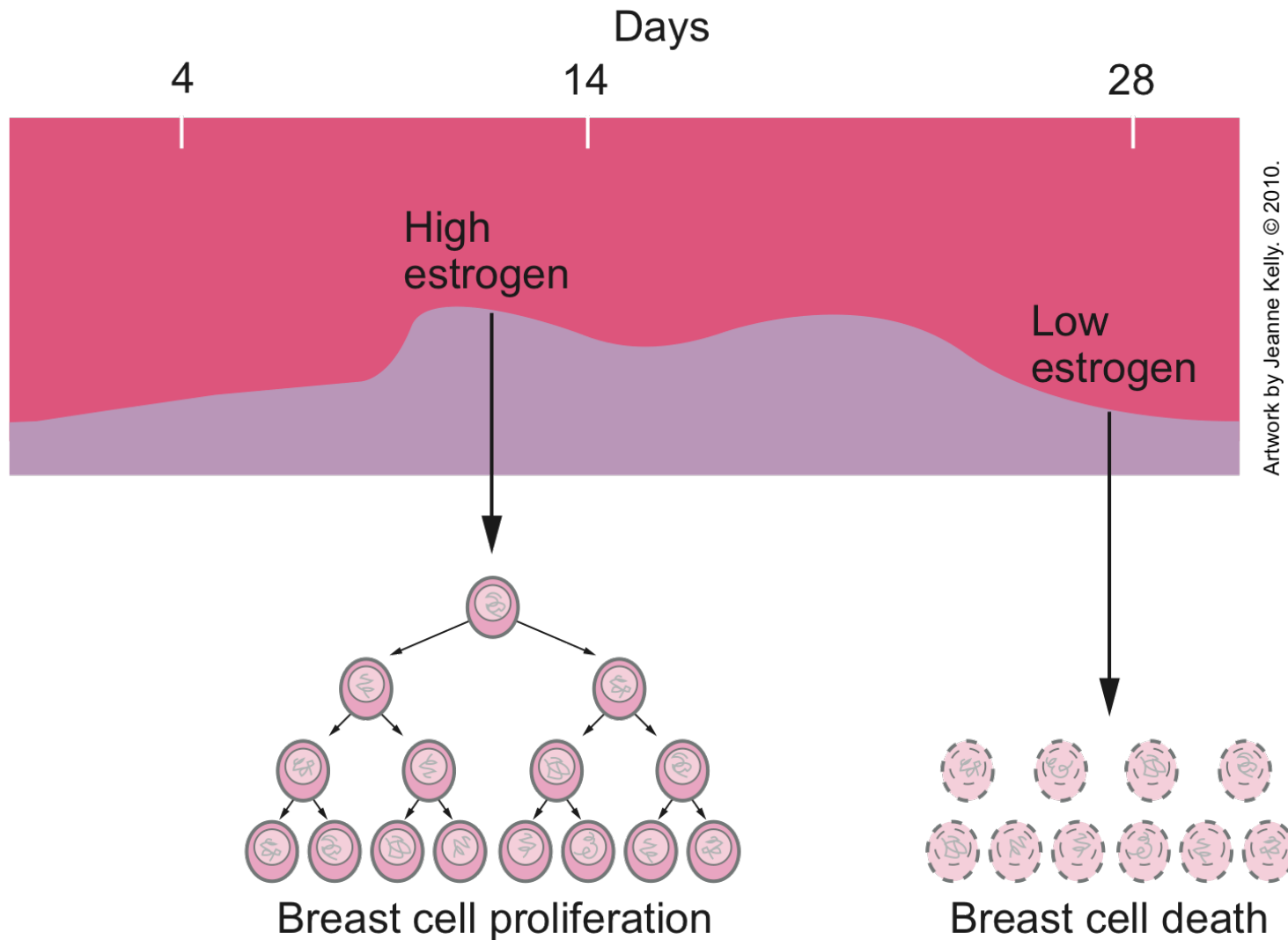
Estrogen and Cancer



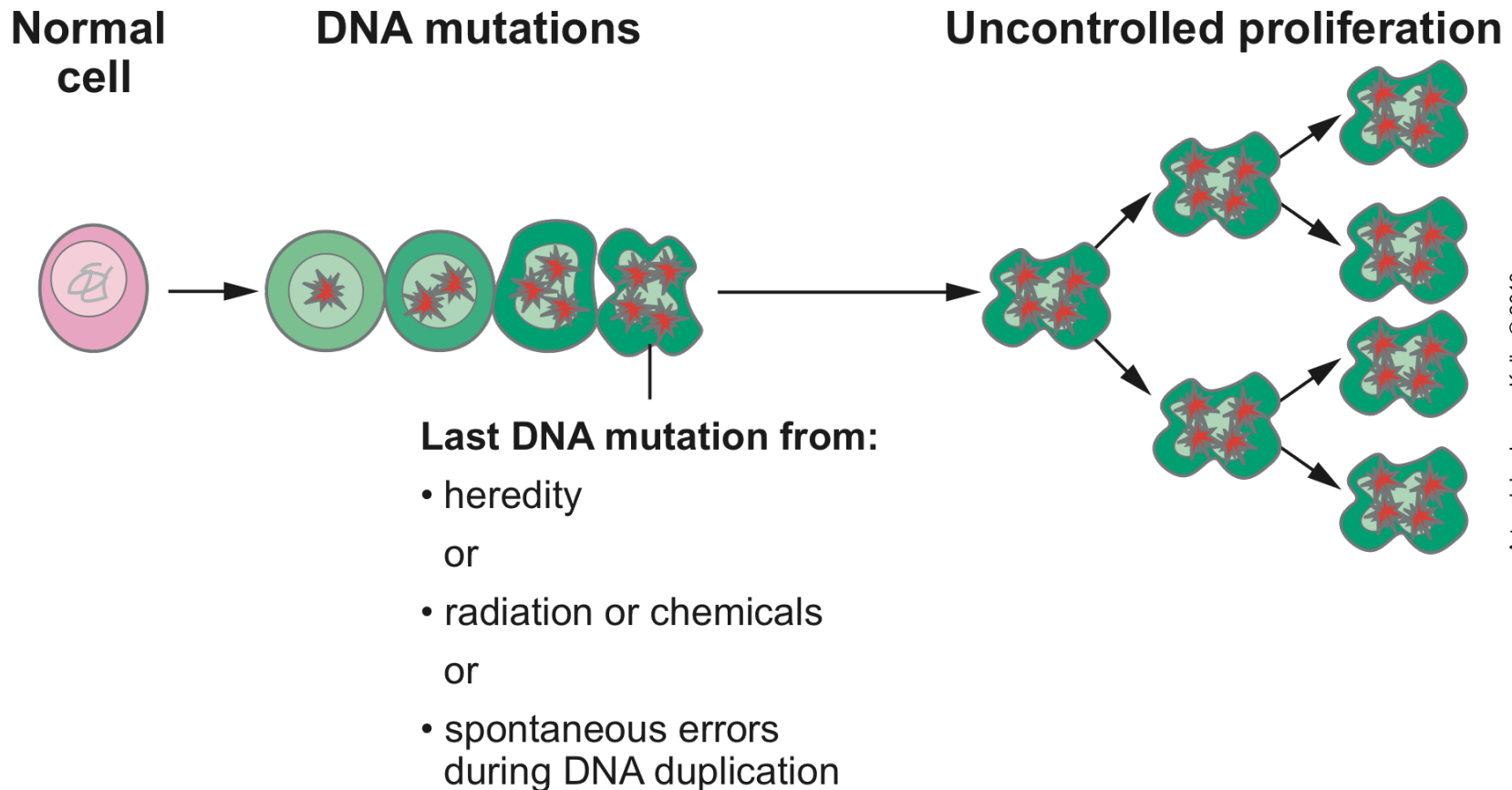
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Estrogen and Breast Cancer

The Menstrual Cycle



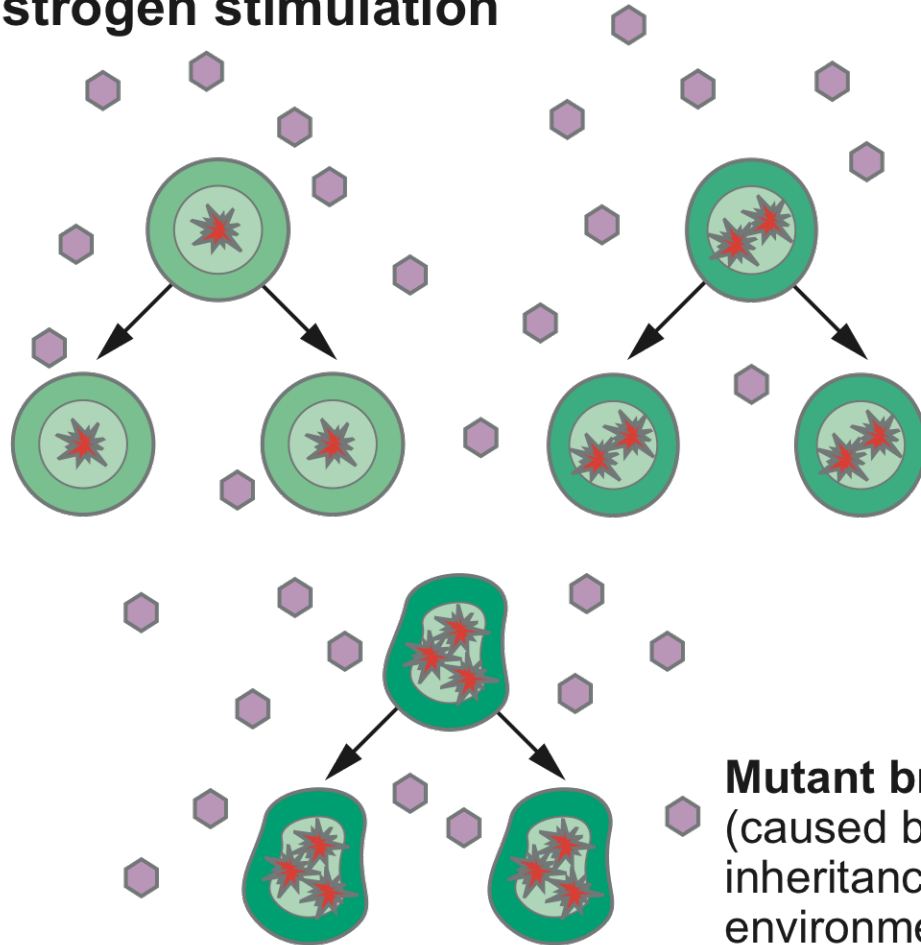
Cancer Arises From DNA Mutations in Cells



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Estrogen-Induced Proliferation of Existing Mutant Cells

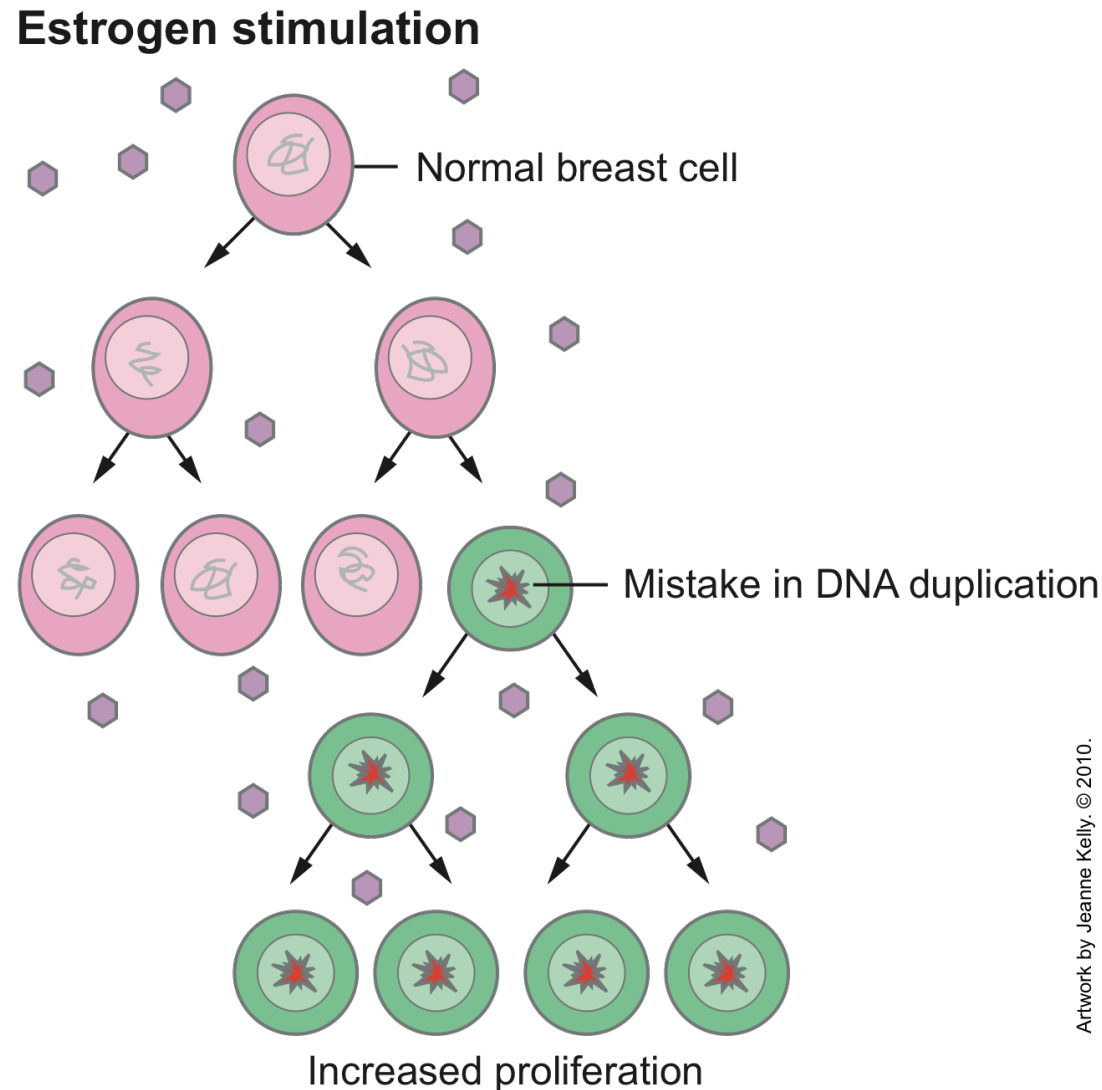
Estrogen stimulation



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Mutant breast cells
(caused by error,
inheritance, and/or
environmental factors)

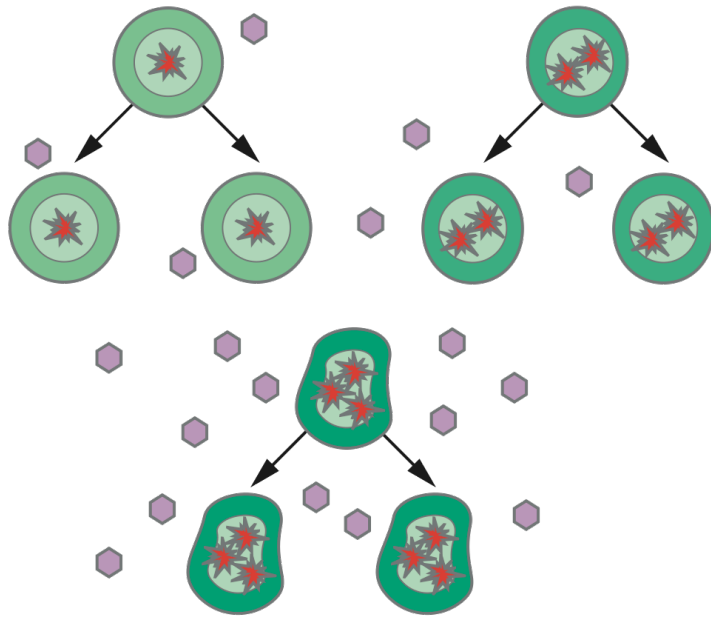
Estrogen-Induced Proliferation and Spontaneous New Mutations



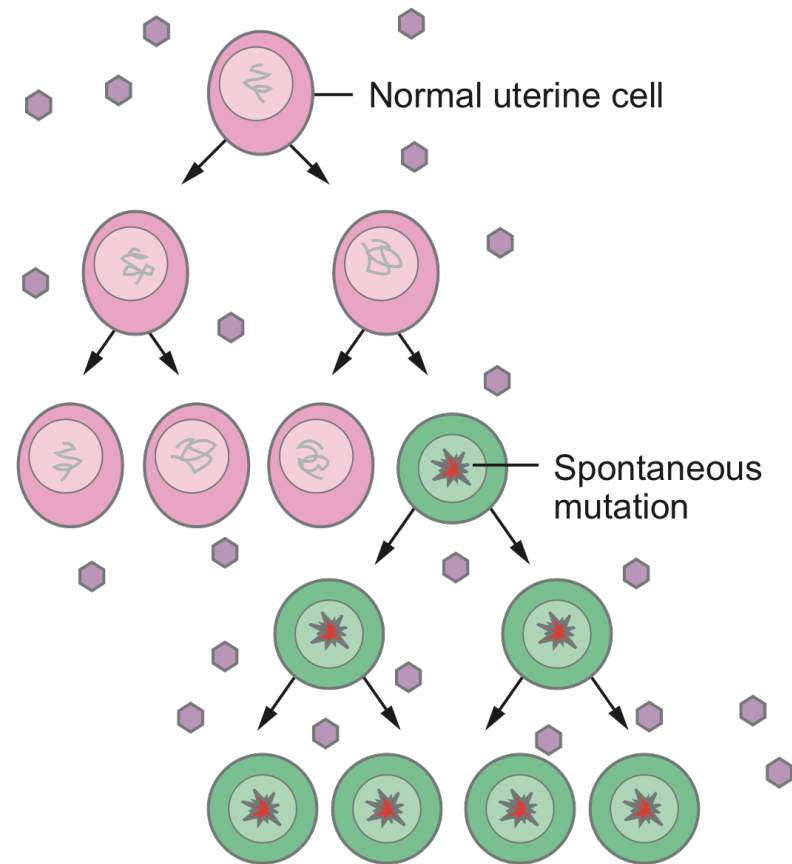
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Estrogen and Uterine Cancer

Estrogen action on the uterus



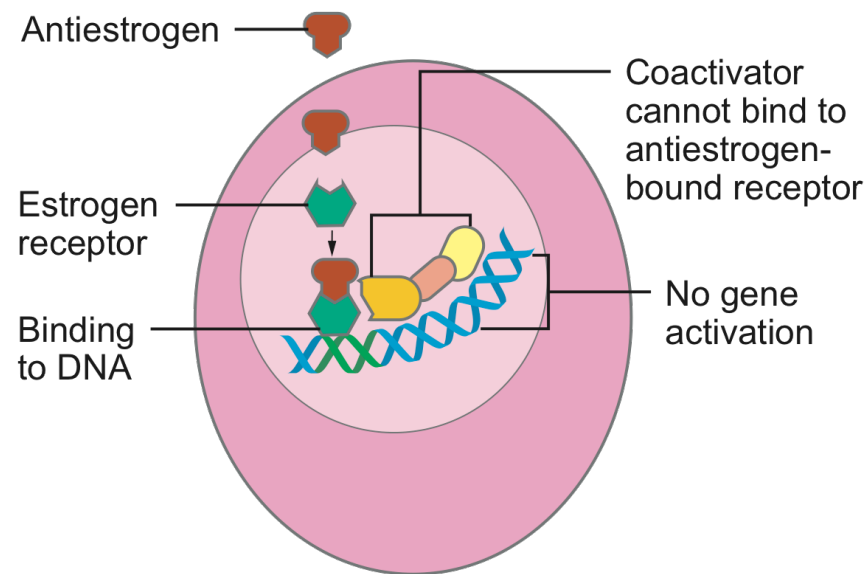
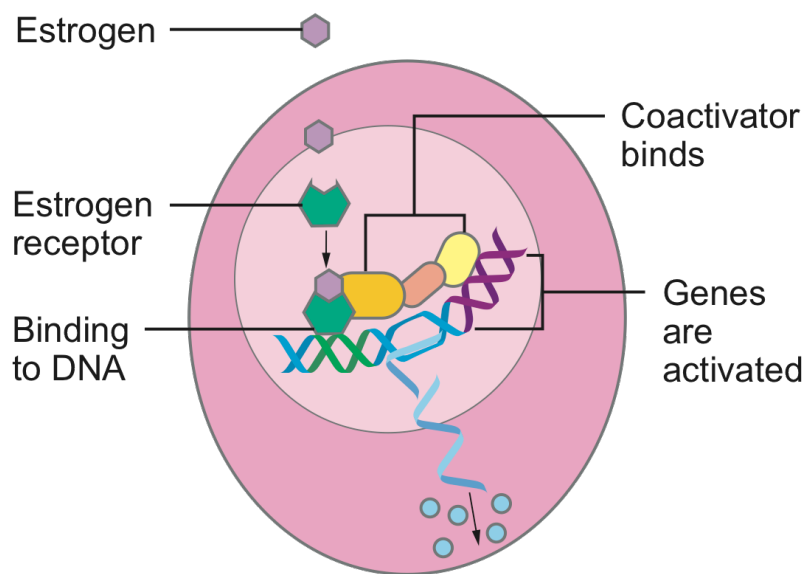
1. Estrogen can stimulate the division of existing mutant uterine cells.



2. Estrogen can increase the chances of developing new, spontaneous mutations.

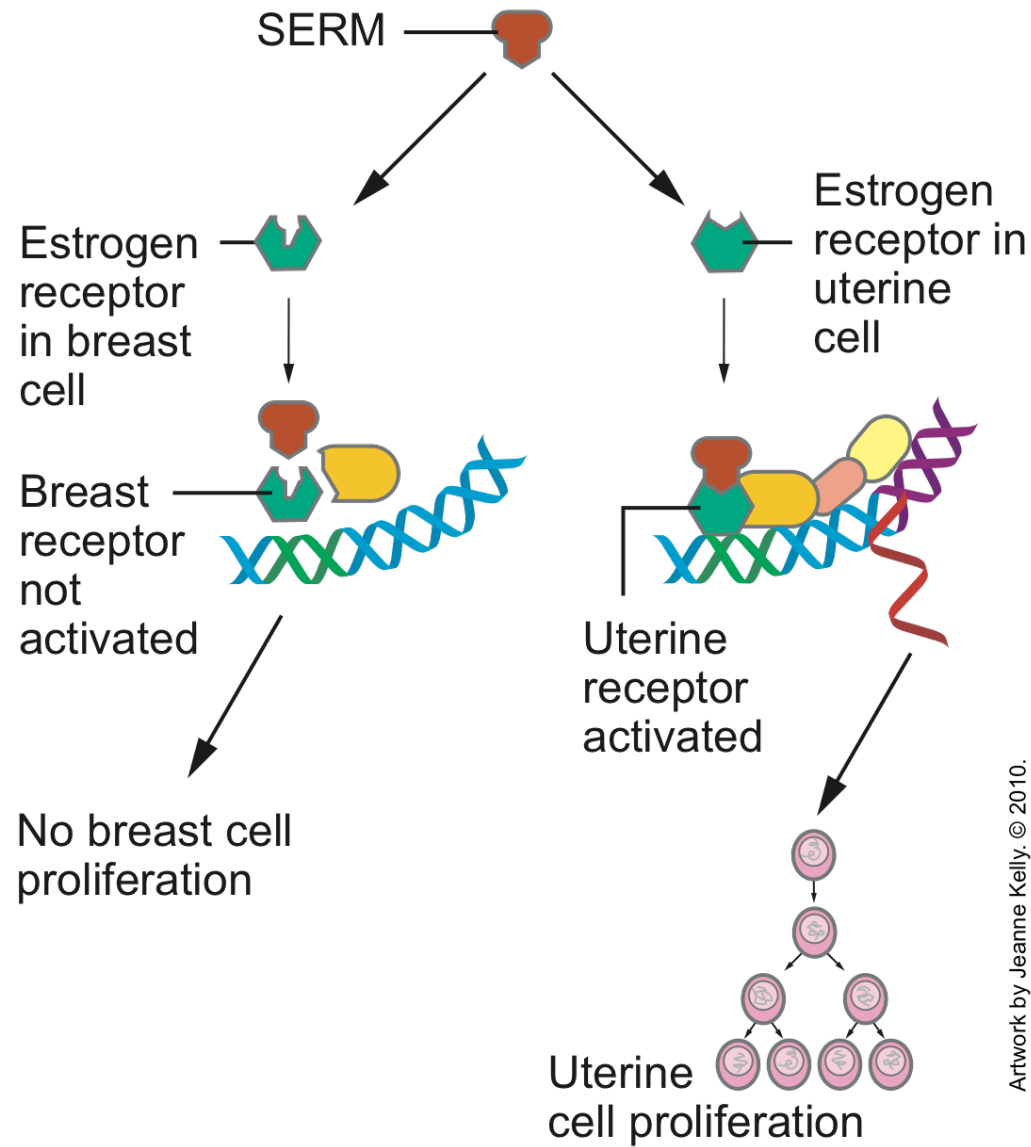
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Antiestrogens



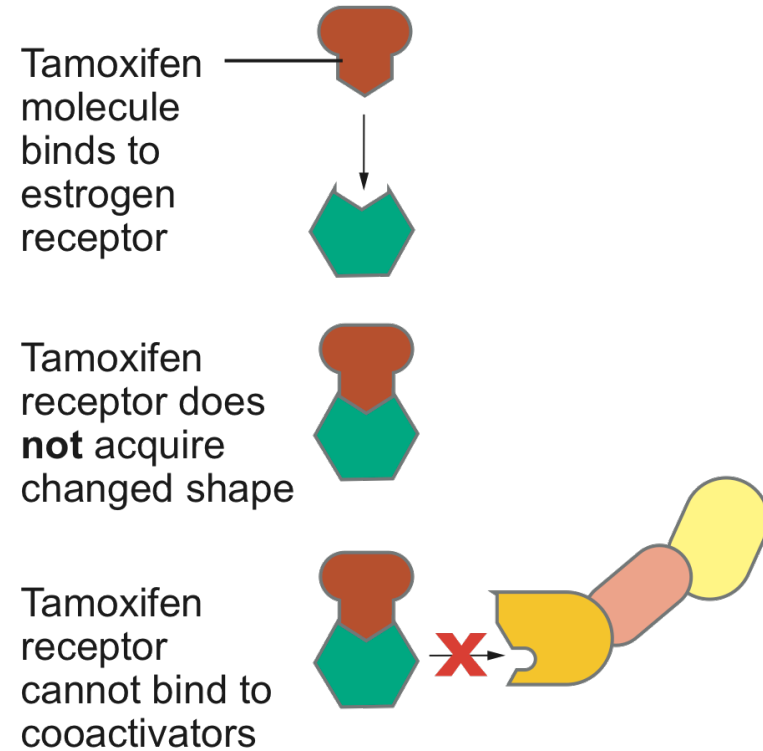
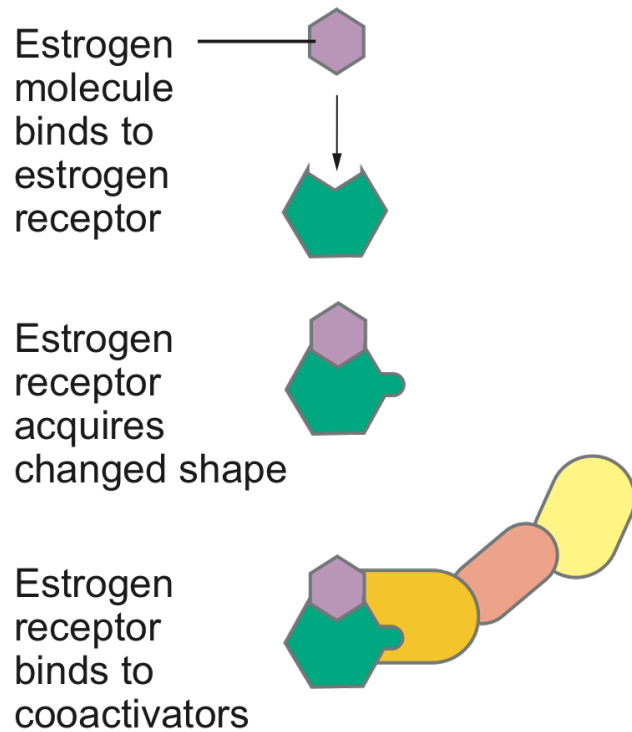
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SERMs



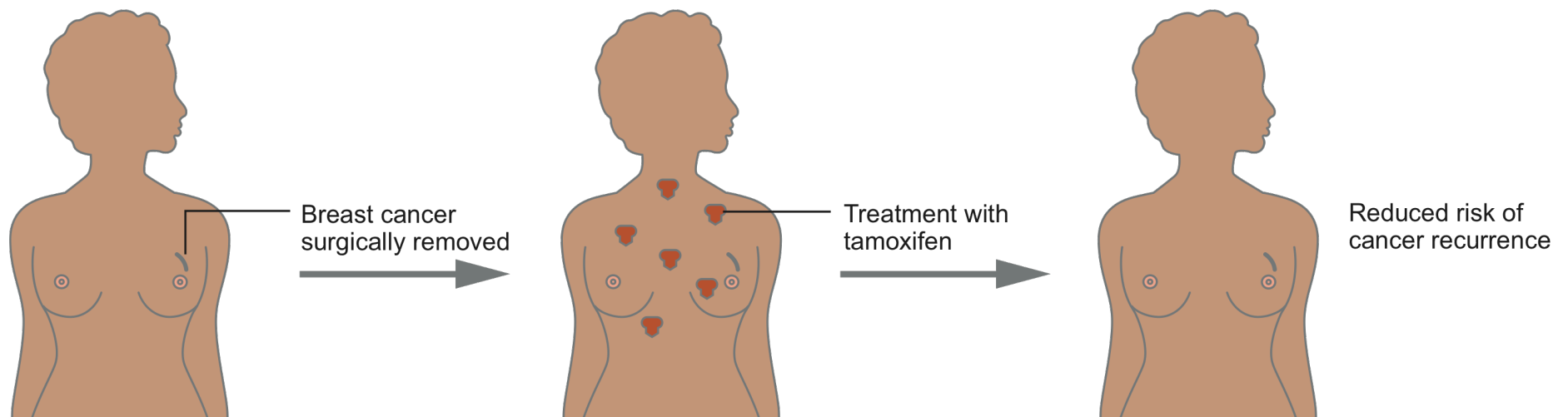
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Tamoxifen and Cancer



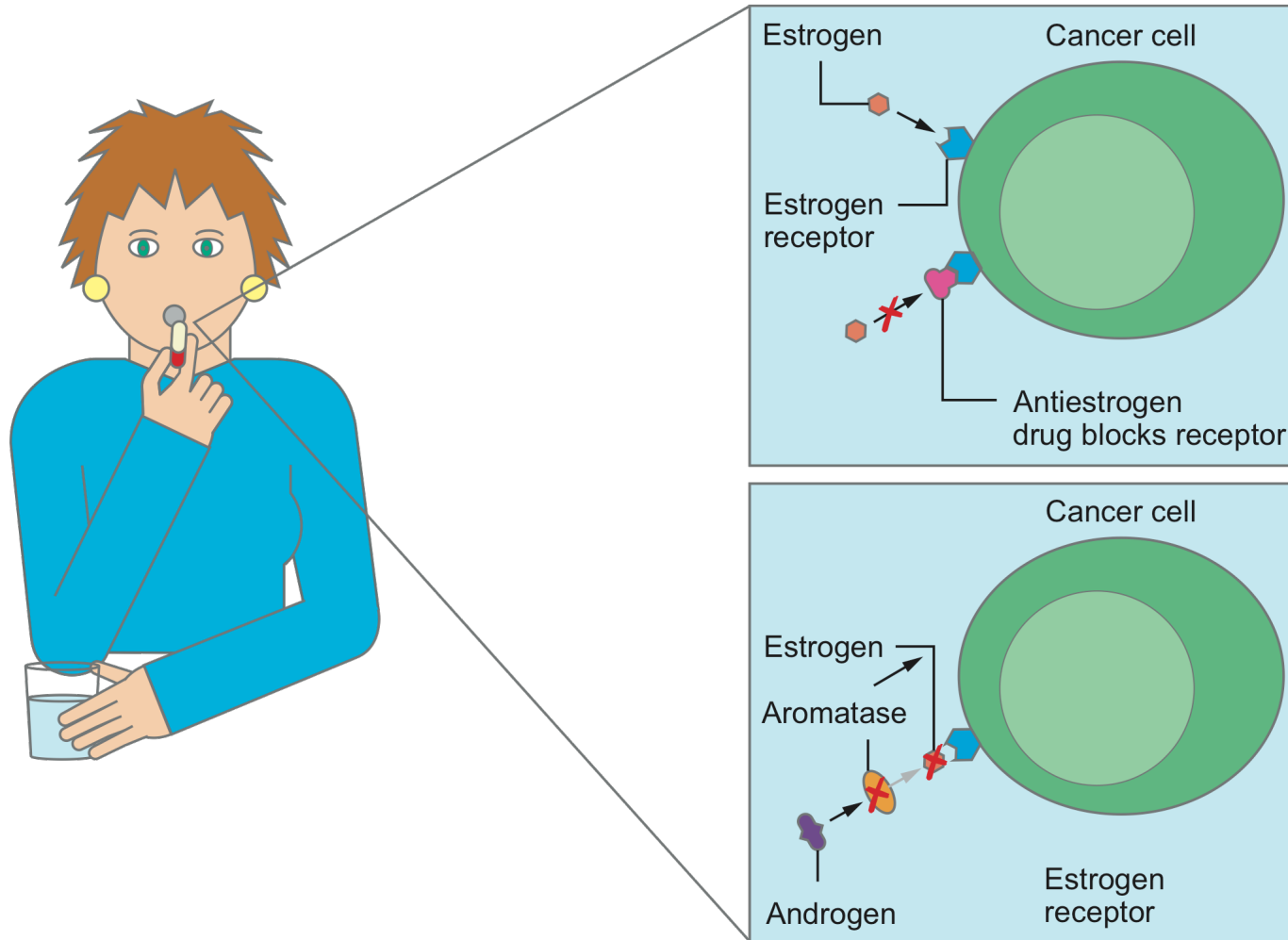
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Tamoxifen and Breast Cancer Treatment



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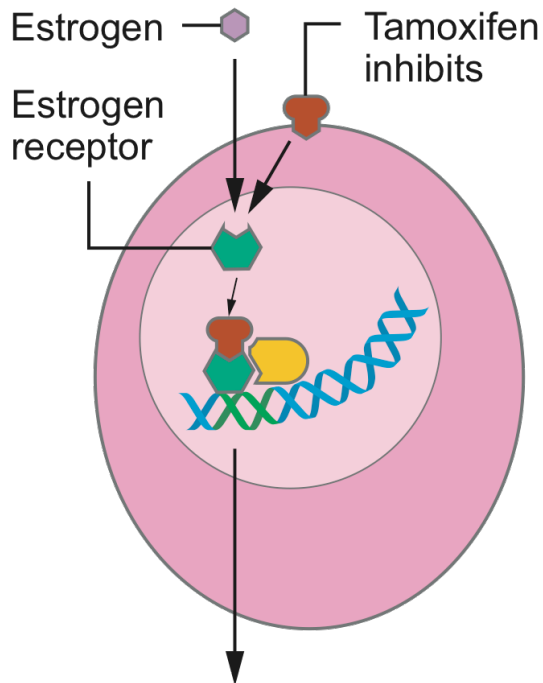
Aromatase Inhibitors



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Estrogen Receptor-Negative Breast Cancer

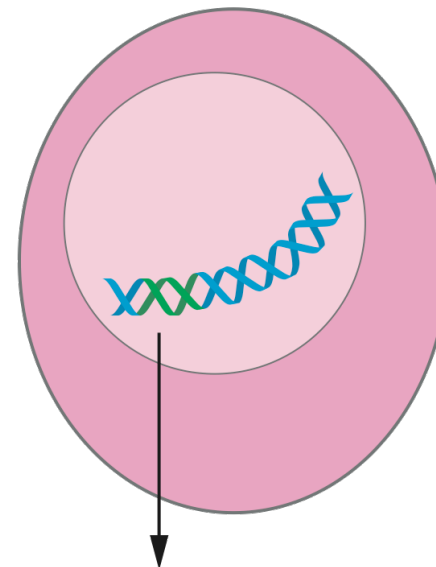
Estrogen receptor-positive breast cancer



Cell proliferation

- Controlled by estrogen
- Inhibited by tamoxifen

Estrogen receptor-negative breast cancer

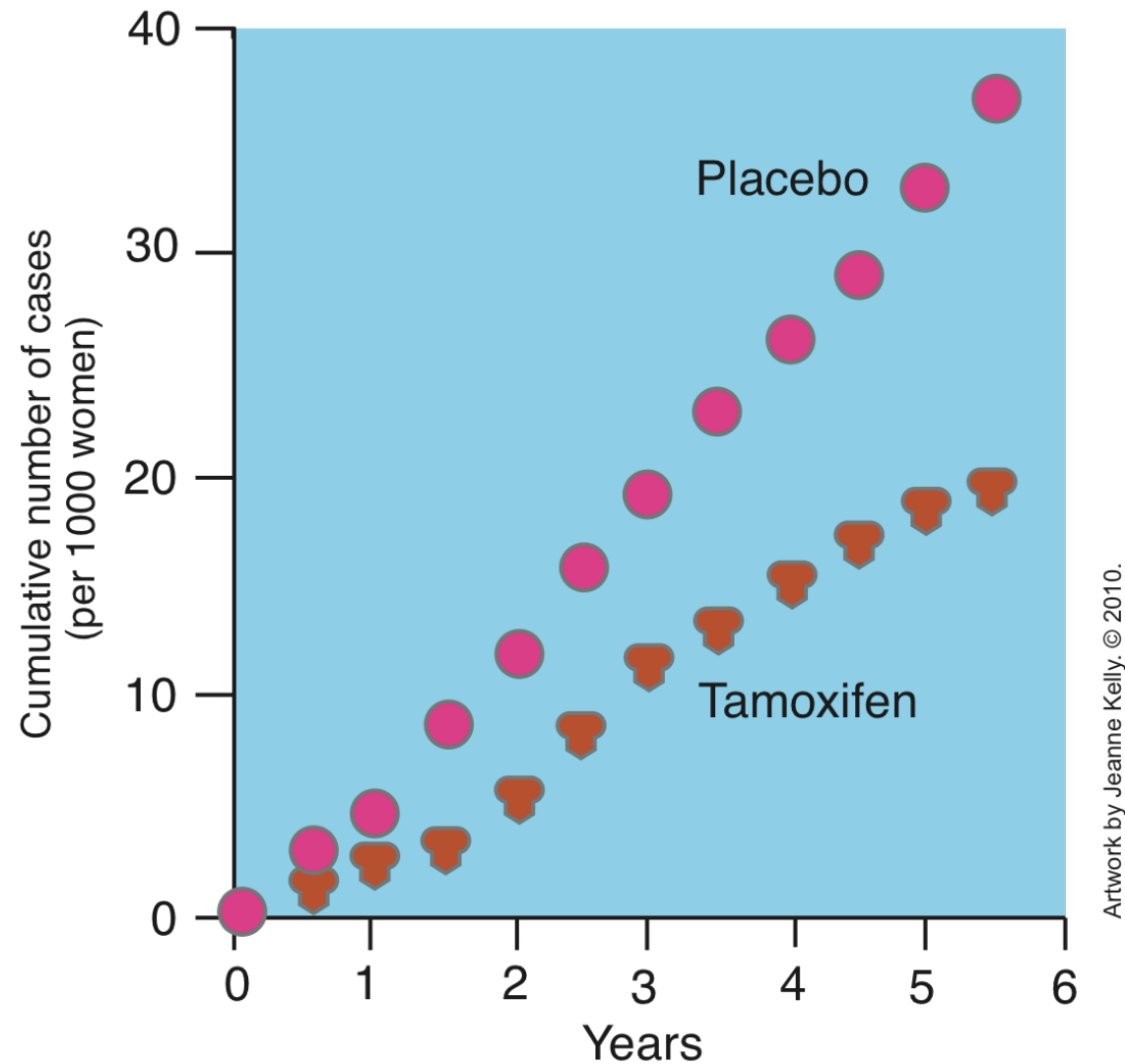


Cell proliferation

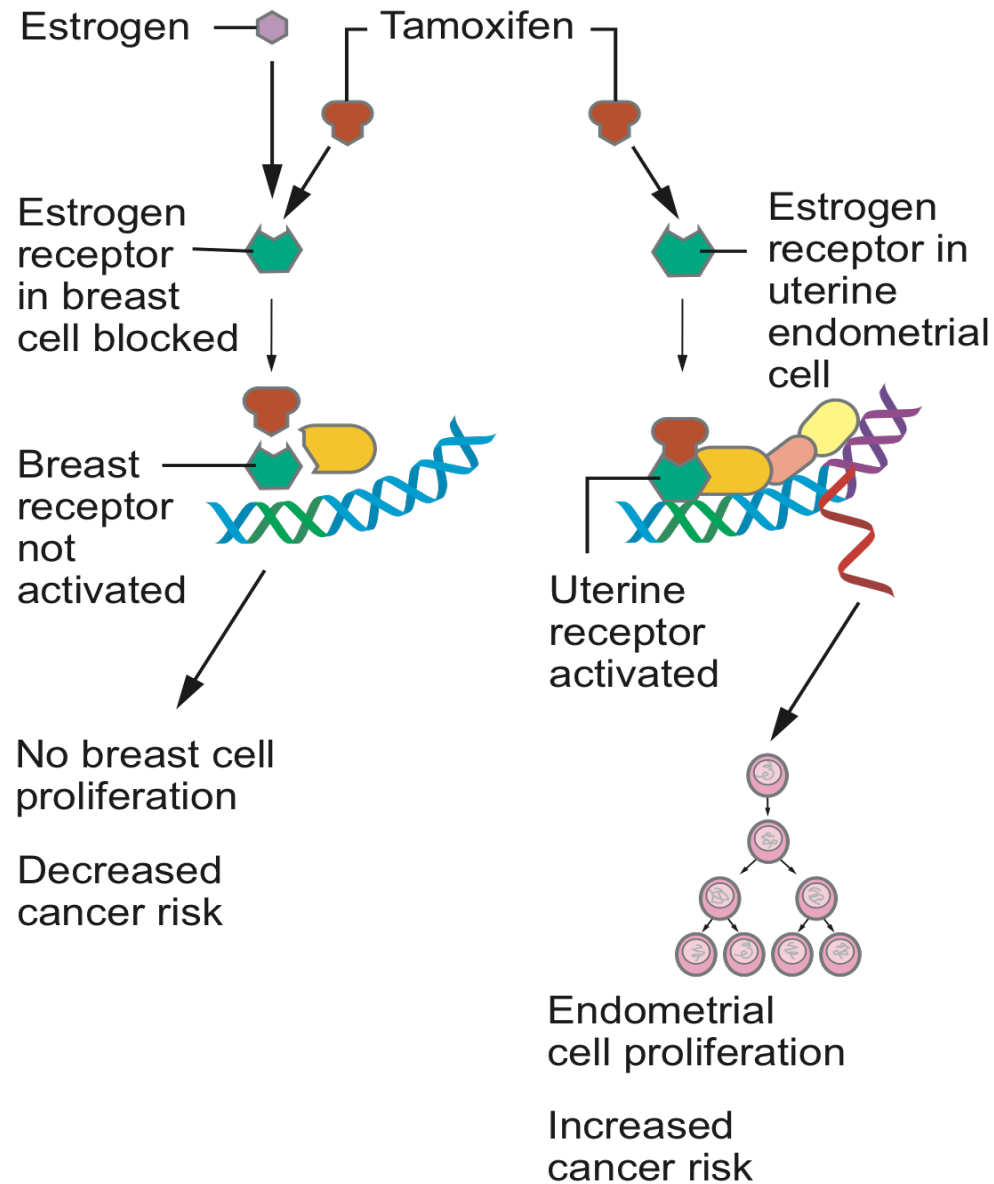
- Not controlled by estrogen
- Not inhibited by tamoxifen

Tamoxifen and Breast Cancer Prevention

Invasive breast cancer rates in women at high risk

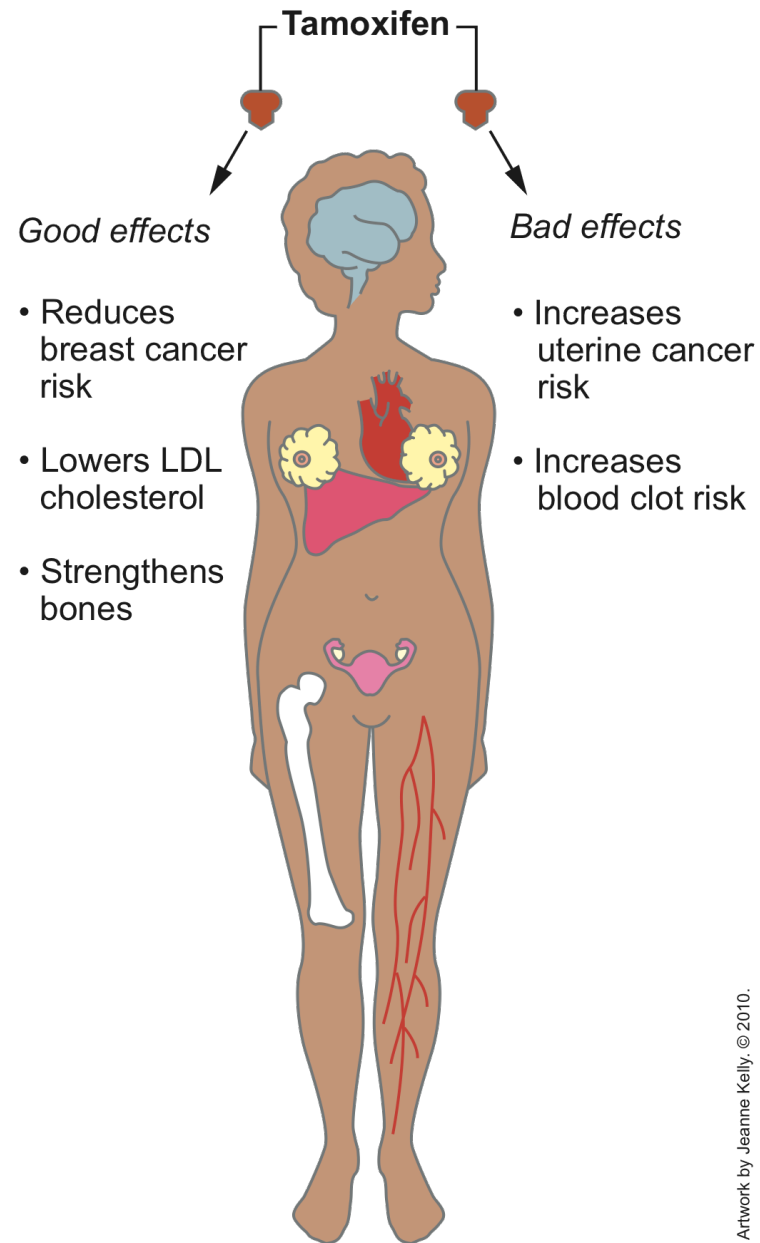


Tamoxifen as a Cause of Uterine Cancer



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The Need for Better SERMs



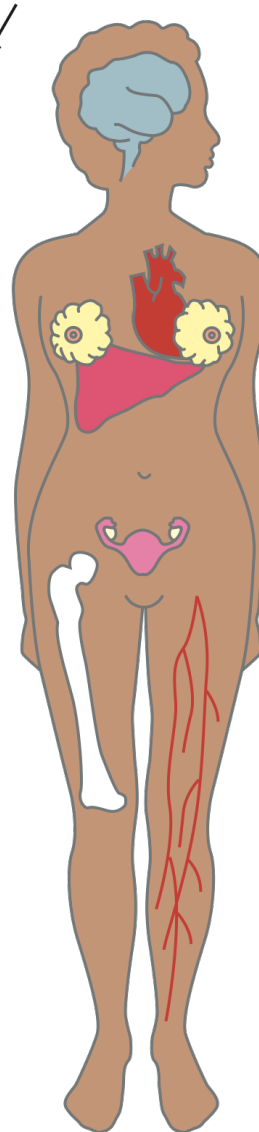
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Estrogen Replacement in Menopause

Estrogen effects associated with hormone replacement therapy during menopause

Good effects

- Strengthens bones
- Lowers LDL cholesterol
- Raises HDL cholesterol
- Reduces menopausal symptoms (e.g., hot flashes)

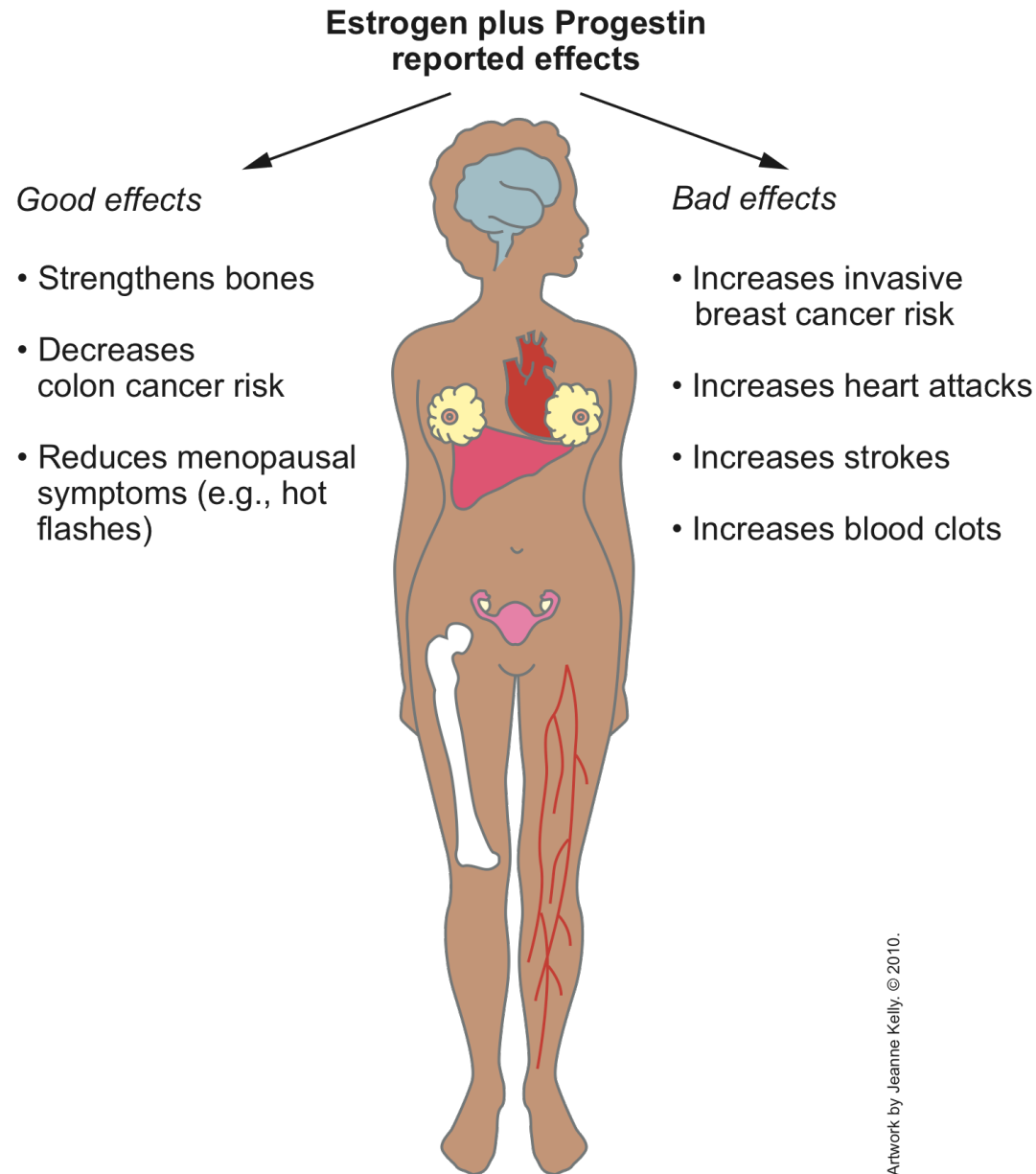


Bad effects

- Increases breast cancer risk
- Increases uterine cancer risk
- Increases blood clot risk

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Estrogen Plus Progestin Replacement



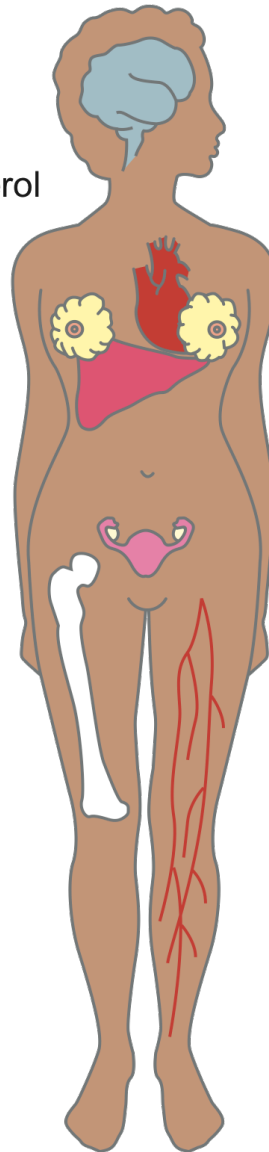
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Search for the Perfect SERM

The “ideal” SERM would:

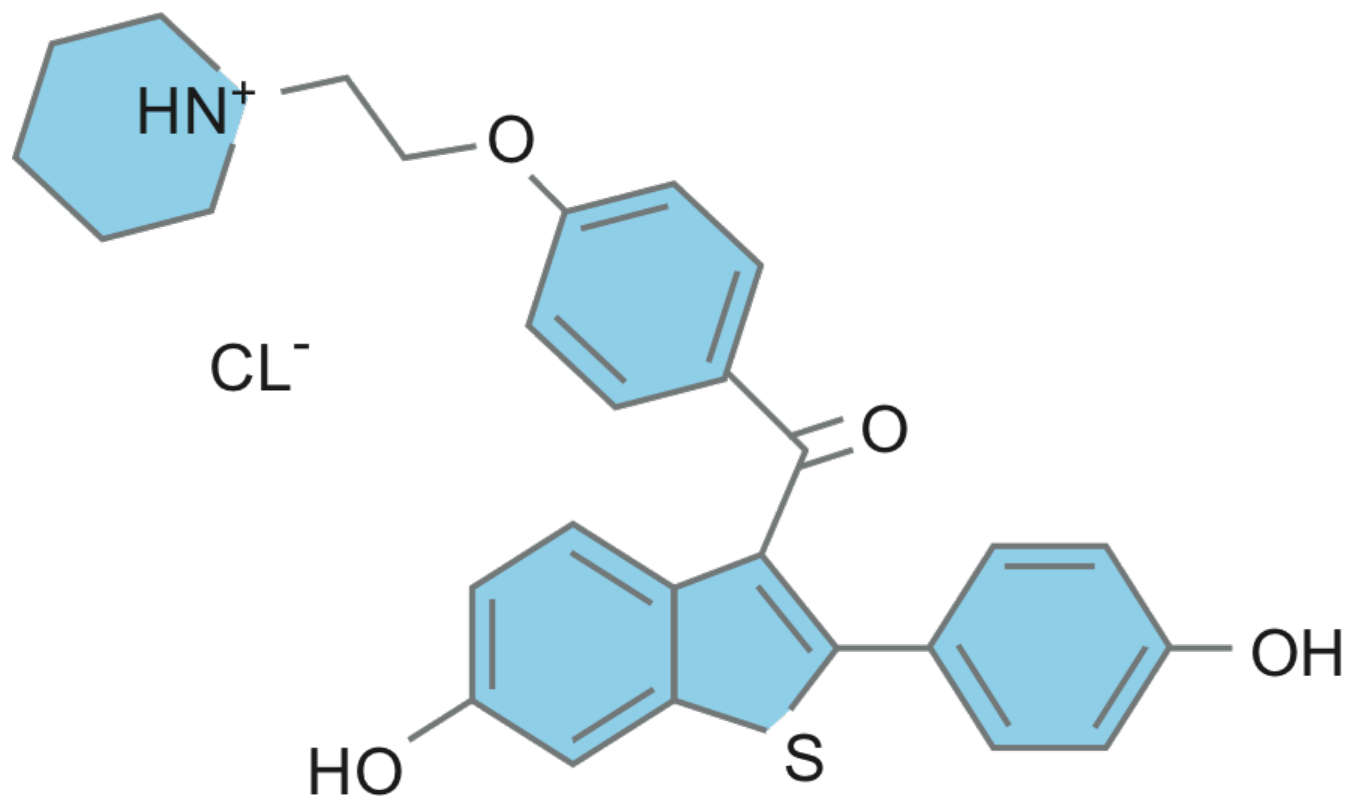


- Strengthen bones
- Lower LDL cholesterol and raise HDL cholesterol
- Relieve hot flashes
- Reduce breast cancer risk
- Reduce uterine cancer risk



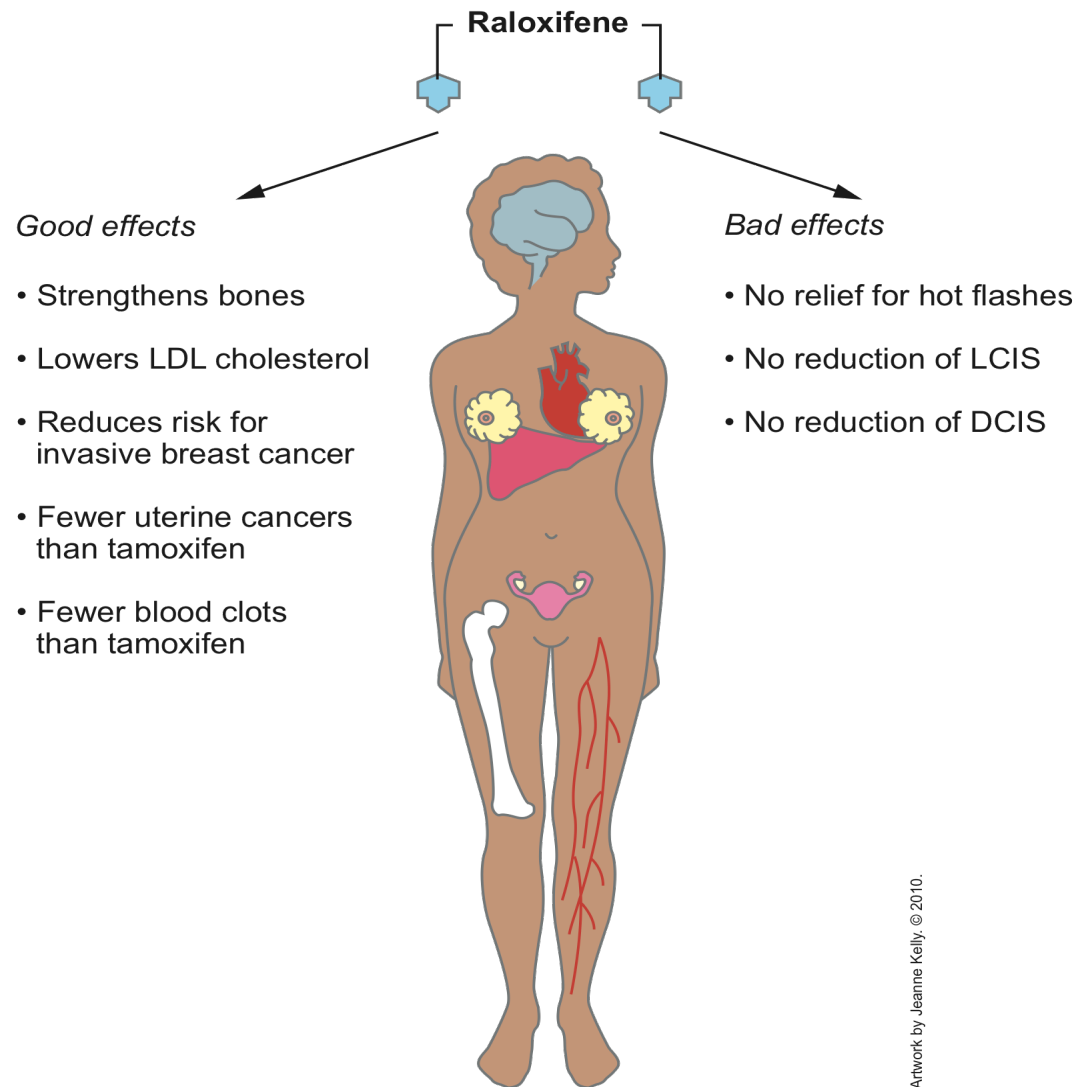
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Raloxifene and the Prevention of Osteoporosis

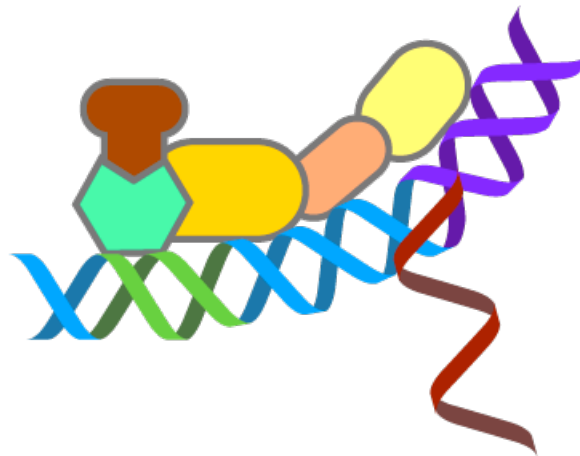


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Raloxifene and Risk of Invasive Breast Cancer



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